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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/039,957	03/16/98	KORNBLITH	P 2509-970451

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1623	14

DATE MAILED: 03/30/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/039,957	Kornblith
Examiner	**Group Art Unit**
Ralph Gitomer	1623

☒ Responsive to communication(s) filed on *Mar 13, 1900*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 3-7, and 9-22* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 3-7, and 9-22* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The CPA request received 3/13/00 has been entered and claims 1, 3-7, 9-22 are currently pending in this application. The after final amendment received 2/17/00 has not been entered as confirmed in a phone conversation with Mr. Thomas Clinton on 3/27/00. The amendment of 2/17/00 was not entered because entirely new subject matter was added to the claims requiring further consideration regarding new matter and issues under 35 USC 112 and further searching. Therefore, the previous final rejection is maintained.

It is understood the present claims are directed to non-malignant cells whereas the claims of 08/679,056 and 09/095,993 are directed to malignant cells. As the function of the methods are identical, the method steps are identical, and the only difference is the state of the cells in the assay, the following rejection is made under obviousness double patenting.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re*

Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-7, 9-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of copending Application No. 09/095,993. Although the conflicting claims are not identical, they are not patentably distinct from each other because the only difference in the claimed methods is the state of the cells being malignant or non-malignant.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3-7, 9-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,728,541. Although the conflicting claims are not identical, they are not patentably distinct from each other because the only difference in the claimed methods is the state of the cells.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-7, 9-22 are rejected under 35 U.S.C. 102(b) as being anticipated by each of Yen-Maguire, Stampfer, Morgan and Rotman.

Yen-Maguire (5,242,806) entitled "Method for Conducting the Cytotoxicity Assays on Tumor Cells" teaches in the abstract, assaying for the sensitivity of biopsied tumor cells to chemotherapeutic agents. In column 3 first full paragraph, measuring the responsiveness of multiple cell populations rather than single-cell suspensions. In column 3 lines 56-59, the requirement for single cell suspensions is eliminated. In column 10 lines 20-25, even if cells are seeded as aggregates, the cells will spread out.

Stampfer (4,423,145) entitled "Enhanced Growth Medium and Method for Culturing Human Mammary Epithelial Cells" teaches in column 3 under "Isolation of Epithelial Clumps," clumps of cells are obtained from a biopsy and then cultured. In column 6 last full paragraph, adriamycin sensitivity to specimens are determined with varying concentrations.

Morgan (5,270,172) entitled "Method to Predict Tumor Response to Therapy" teaches in column 5 Example 1, cancer tissue obtained is minced into fragments and cultured. In column 13 last full paragraph, chemotherapeutic drugs and doses are assayed.

Rotman (4,937,187) entitled "Methods for Separating Malignant Cells From Clinical Specimens" teaches in column 8 in the claims generally and claim 19 specifically, forming clumps of cells from tumor biopsies, establishing a cell culture, exposing the cell culture to a therapeutic agent and determining the sensitivity of the cells to the agent.

It would appear the inventive step is to not disaggregate a biopsy specimen into individual cells before plating but to plate clumps of cells prior to determining chemotherapeutic sensitivity. However, this is not claimed as the present claims are written in open-ended "comprising" terminology which does not exclude disaggregating the specimen and "multicellular particulates" does not define a size of specimen. Mechanically separating as has now been added to the claims is clearly shown in all of the above references where biopsying itself is a method of mechanically separating.

Applicant's arguments filed 8/18/99 have been fully considered but they are not persuasive.

Applicant argues that Yen-Maguire may further process the cells to disaggregate them. Stampfer does not mechanically separate the cells. Morgan does not describe passaging a monolayer derived from the particulates but a suspension instead. Rotman also does not describe passaging a monolayer derived from the particulates.

It is the examiner's position that the claims do not exclude further processing to disaggregate cells because they are written in open-ended ▒comprising▒ terminology. Stampfer inherently mechanically separates cells, see column 3 lines 14-20 where samples are prepared by gently lacerating the remaining tissue with opposing scalpels after additional dissection. The present claims are not directed to passaging a monolayer. Morgan in Example I columns 5-6 teaches a thin layer of cells on a slide is grown. Tissue culture monolayer is well known in this art and would have the expected function. In Rotman, see the abstract where fragments from biopsy sample can be prepared by mechanical dissociation.

Claims 10 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 10 is directed to a wound healing agent and claim 17 is directed to a gene therapy agent.

The specification as originally filed does not enable one of skill in this art to make and use the presently claimed invention as directed to wound healing and gene therapy agents.

Claims 1, 3-7, 9-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The newly added limitation directed to non-malignant cells is not enabled. On page 6 first full paragraph of the present specification, applications of the invention are discussed including screening process for treatment or therapeutic agents for nonmalignant syndromes and psoriasis or wound healing agents as examples are disclosed. The claims are directed to assessing chemosensitivity of non-malignant cells, a method for identifying chemosensitivity of cells, and a method for identifying secreted cellular antigens produced by cells. The specification as

originally filed does not provide a written description nor enable one of skill in this art how to assess chemosensitivity of non-malignant cells, identify chemosensitivity of cells nor identify any secreted cellular antigens produced by cells. No results of any of these processes are disclosed, and particularly no non-malignant cells are shown. It is understood psoriasis is not a malignant condition but nowhere is it set forth in the specification what the sensitivity of cells associated with psoriasis are chemosensitive to, how one would identify that sensitivity or any antigens produced by those cells. No results of any kind are seen.

Claims 13-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for for specific markers or factors, does not reasonably provide enablement for any marker or factor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In claim 13 and all occurrences, the terms "soluble secreted factors", in claim 14 "cellular markers", in claim 21 "biological response modifier" lack enablement as it would require one of ordinary skill in this art undue experimentation to determine which such factor, marker or modifier would work in the instant invention.

"Soluble secreted factors" reads on air which is unlikely to work in the claimed invention.

"Cellular markers" reads on utilization of a nutrient which is unlikely to work in the claimed invention.

"Biological response modifier" reads on air which is unlikely to work in the claimed invention.

The entire scope of the claims has not been enabled because:

1. Quantity of experimentation necessary would be undue because of the large proportion of inoperative compounds claimed.
2. Amount of direction or guidance presented is insufficient to predict which substances encompassed by the claims would work.
3. Presence of working examples are only for specific substances and extension to other compounds has not been specifically taught or suggested.
4. The nature of the invention is complex and unpredictable.
5. State of the prior art indicates that most related substances are not effective for the claimed functions.
6. Level of predictability of the art is very unpredictable.
7. Breadth of the claims encompasses an innumerable number of compounds.
8. The level of one of ordinary skill in this art is variable.

In re Wands, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

Applicant's arguments filed 8/18/99 have been fully considered but they are not persuasive.

All arguments regarding 35 USC 112, first paragraph, will be considered here.

Applicant argues that the purpose of the assays is to determine whether a chemical could affect the cells cultured through use of gene therapy or wound healing agents. The treatment would yield expected results determined by the nature of the treatment. The treatment method would have already been known to the skill artisan, if not, there would be no incentive to test the agent in its wound healing or gene therapy capacity. Selection of candidate agents is routine. The specification teaches harvesting separating, growing, inoculating, treating and assessing. The claims have been amended to clarify that the detection of the markers or factors is indicative of a disease state and that the markers, factors or modifiers are products of or characteristics of the cells.

It is the examiner's position that the claims are not directed to gene therapy or wound healing agents. This rejection is not based upon how the candidate drugs are selected but that the specification does not enable one to obtain the results claimed. No agents for wound healing or gene therapy are disclosed, no chemosensitivity of non-malignant cells is taught, no chemosensitivity is identified and no secreted cellular antigens are identified. Importantly, no non-malignant cells are

disclosed. That the method steps are shown does not enable the claimed method. Regarding the markers or factors, it would appear what the markers or factors may be is critical to the invention and what is disclosed does not enable the scope of the claims.

Claims 1, 3-7, 9-22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of claim 1 is directed to assessing chemosensitivity of cells but the claim lacks any such step. In claim 1(e) sites are treated with treating means which is not related to chemosensitivity, no determining takes place, and correlating sensitivity occurs which is not understood. In claim 3 ▒said plurality of segregated sites▒ lacks antecedent basis. In claim 4 and all occurrences ▒active agent▒ lacks antecedent basis and is not understood as to what activity is intended. In claim 4 how the assessment takes place is indefinite and it is not seen how one could determine optimal sensitivity to a single agent in the presence of many agents. In claim 9 ▒a chemotherapeutic agent▒ would imply malignancy is being treated which is inconsistent. In claim 11 ▒radiation therapy would imply malignancy is being treated which is inconsistent. Claims 15, 16 and all related occurrences does not contain steps to

accomplish the preamble. In claim 16(c) and all occurrences, ▒said cohesive multicellular particulates▒ lacks antecedent basis.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (703) 308-0732. The examiner can normally be reached on Tuesday-Friday from 8:00 am - 5:00 pm. The examiner can also be reached on alternate Mondays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Geist can be reached on (703) 308-1701. The fax phone number for this Art Unit is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1234.

Ralph Gitomer
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